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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,573	05/25/2001	John S. Haurum	4305/1 J396-US1	4477

7278 7590 03/07/2002

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EXAMINER	
JAMROZ, MARGARET E	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/866,573	HAURUM ET AL.	
	Examiner	Art Unit	
	Margaret E Jamroz	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-14 and 23-34* is/are pending in the application.

4a) Of the above claim(s) *23-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 5-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5 and 10*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's amendment, filed 1/22/02 (Paper No. 9), is acknowledged.

Claims 1, 5-14, and 23-34 are pending.

Applicant's election with traverse of Group I (claims 1 and 5-14) in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the addition of groups VII and VIII (methods of using the composition of Group I) does not constitute an undue burden. This is not found persuasive because a composition can be set apart from its method of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product of groups I can be used in a materially different process, such as affinity chromatography, in addition to the methods or treating or preventing allergy or inducing tolerance.

The requirement is still deemed proper and is therefore made FINAL.

Claims 23-34 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to non-elected inventions.

Claims 1 and 5-14 are under consideration in the instant application.

2. Claims 10-12 are objected to for depending on canceled claim 2.

3. The abstract of the disclosure is objected to because:

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The

abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1 and 5-14 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising a recombinant polyclonal IgM or IgA for administration to mucosal surfaces, does not reasonably provide enablement for a pharmaceutical composition comprising any other isotype of recombinant polyclonal antibody capable of binding allergen for administration to mucosal surfaces. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

The claims as written encompass every isotype of antibody including IgM, IgA, IgG1, IgG2a, IgG2b, IgG3, IgD, and IgE.

It is well known in the art that only IgM and IgA are capable of transport across mucosal surfaces. Roitt et al. (Immunology, Harper and Row, Publishers, New York, 1989, pages 5.5-5.6 and 3.8) due to the presence of J chain that is lacking in the other isotypes. Pharmaceutical compositions comprising recombinant polyclonal IgG1, IgG2a, IgG2b, IgG3, IgD, and IgE would not be able to cross mucosal surfaces, and therefore, applicant has not taught how to make or use a pharmaceutical composition for topical application to any mucosal surface with said isotypes.

Applicant is relying upon certain biological activities and the disclosure of a limited representative number of species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated immunoglobulin isotypes lacking a J chain would be expected to have greater differences in their activities. For it is noted that IgM/IgA and IgG1/IgG2a/IgG2b/IgG3/IgD/IgE do not share critical common structural attributes (i.e. the J chain), as the isotypes differ with respect to their structural and physiochemical properties.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

6. Claims 1 and 5-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of a pharmaceutical composition comprising a recombinant polyclonal IgM or IgA for administration to mucosal surfaces.

Applicant is not in possession of a pharmaceutical composition comprising any other isotype of recombinant polyclonal antibody capable of binding any allergen for administration to any mucosal surfaces.

Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated recombinant polyclonal antibodies recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993). A description of a genus of recombinant polypeptide antibodies may be achieved by means of a recitation of a representative number of polypeptide antibodies, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 5, 9-12 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 5,789,208.

The '208 patent teaches a pharmaceutical composition comprising recombinant polyclonal antibody libraries using phage display libraries with a pharmaceutically acceptable carrier in solution which may be disease-specific, patient-specific, or both (see the Abstract; column 8, paragraph 1; column 16, paragraph 2; and the claims in particular). The composition is free of any allergen. The recombinant polyclonal antibody is generated by linking the immunoglobulin (Ig) heavy chain variable region (V_H) and light chain variable region (V_H) and in a parental library in order to allow for the bulk transfer of V_L and V_H pairs from one vector to another, thus making a complete polyclonal antibody (see columns 5-6, columns 11-15, and columns 26-29 in particular). The '208 patent teaches a method of using cDNA and PCR to link and amplify V_H and V_H and recovering the linked combinations from supernatants (see column 6, paragraphs 3-4 in particular). One advantage of the recombinant polyclonal libraries is that "once isolated and cloned, the library can be expanded to ensure the representation of every member of the antigenic profile and can also be easily transferred to other vectors (see column 7, paragraph 4 in particular). More specifically, the'208 patent teaches a method for preparing a first library of expression vectors comprising paired nucleic acid fragments, said paired nucleic acid fragments being suitable for transfer to prepare a second library of different expression vectors; and further, wherein the plurality of segments in the first cassette can be transferred into a plurality of second vectors to produce a second library of expression vector molecules. The methods recited in the '208 patent claims can be use to produce an antibody (claims 1-26 in particular). The resulting recombinant antibody may be one of many human or murine isotypes, including IgA (i.e. an antibody which binds allergen; see column 13, lines 61-67 in particular).

Therefore, the '208 patent anticipates the claimed invention.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 6-8, and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,789,208 (IDS reference) in view of U.S. Patent 5,670,626 (IDS reference).

The '208 patent has been discussed supra. Further, the'208 patent teaches that recombinant polyclonal antibodies are advantageous because they overcome some of the drawbacks associated with monoclonal antibody therapy, are directed to many different antigenic determinants, and can be made on a much larger scale than Ig in gamma globulin (see column 5 in particular).

The '208 patent does not teach a recombinant polyclonal antibody which is capable of effecting topical application (claims 6-8), or wherein the allergen to which the antibody binds is selected from the group recited in claim 13, or comprising an amount in the range of 1 μg to 1g per unit dosage form as recited in claim 14.

The '626 patent teaches pharmaceutical preparation containing human monoclonal IgA antibodies specific for major allergenic proteins found in ragweed (i.e. a grass pollen), house dust mites, and cat and dog dander in solution with a pharmaceutically acceptable excipient which can be topically applied to mucosal surfaces such as the respiratory tract. Recombinant phage libraries are used to generate the combinatorial V_H and V_L by linking genomic fragments in appropriate plasmids and transfecting cells to express the proteins. The antibodies were prepared in a physiological buffer (i.e. solution) for application to the nose at a concentration of 20 to 1000 μg/ml, which is 1-50 μg of antibody per drop (see the entire document).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the pharmaceutical composition comprising a human recombinant monoclonal IgA antibody specific for ragweed (i.e. a grass pollen allergen), house dust mites, and cat and dog dander in solution with a pharmaceutically acceptable excipient which can be topically applied to mucosal surfaces such as the respiratory tract taught by the '626 patent for the pharmaceutical composition comprising a recombinant polyclonal antibody taught by the '208 patent because both antibodies are made by the same recombinant technology and are IgA.

One of ordinary skill in the art would have been motivated to substitute the the pharmaceutical composition comprising a human recombinant monoclonal IgA antibody useful for topical application taught by the '626 patent for the recombinant polyclonal antibodies taught by the '208 patent because recombinant polyclonal antibodies are advantageous because they overcome some of the drawbacks associated with monoclonal antibody therapy, are directed to many different antigenic determinants, and can be made on a much larger scale than Ig in gamma globulin as taught by the '208 patent.

11. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,789,208 (IDS reference) in view of WO 96/09085 (IDS reference).

The '208 patent has been discussed supra.

The '208 patent does not teach the administration of the pharmaceutical composition as a powder.

The WO 96/09085 document teaches a method for aerosolizing a powdered medicament so that dispersion can reach the distal regions of the lungs (i.e. a mucosal surface) which is "effective for both systemic delivery and for localized delivery to treat diseases of the lung" (i.e. asthma; see pages 1-2 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the powdered medicament taught by the WO 96/09085 document for the polyclonal antibodies in solution made by the recombinant polyclonal libraries taught by the '208 patent to generate an antibody for topical administration.

One of ordinary skill in the art would have been motivated to make a powdered medicament taught by the WO 96/09085 document containing the recombinant polyclonal IgA antibodies taught by the '208 patent to have a powdered medicament that can reach distal sites of a mucosal surface and which is effective for both systemic delivery and for localized delivery to treat diseases of the lung as taught by the WO 96/09085 document.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Megan Jamroz, whose telephone number is (703) 308-8365. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Margaret (Megan) Jamroz, Ph.D.
Patent Examiner
Technology Center 1600
March 1, 2002

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